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Original Research

Short-term effect of latanoprostene bunod monotherapy on reducing intraocular pressure and altering macular microvasculature

Kemal Bayrakçeken[1], Hasan Akgöz[2]
[1] Department of Ophthalmology, Faculty of Medicine, Erzincan Binali Yildirim University, Erzincan
[2] Department of Ophthalmology, Erzurum Regional Training and Research Hospital, Erzurum, Turkey

Abstract

Aim: In this study, we aimed to evaluate the effect of topical latanoprostene bunod (LBN) 0.024% on early intraocular pressure (IOP) and macular microvasculature.

Material and Methods: This retrospective study included 46 eyes of 46 treatment-naive participants with primary open-angle glaucoma disease (POAG) who were initiated on topical LBN 0.024%. IOP values of the patients were compared before and the first month after treatment. Macular and ganglion cell complex thicknesses were evaluated using optical coherence tomography (OCT), and macular vessel density parameters were evaluated using OCT angiography (OCTA). Pre-and post-treatment findings were compared with the paired-sample t-test.

Results: At the time of the first presentation, the mean IOP value of the patients was 26.20±2.84 mmHg. After administration of LBN 0.024%, the mean follow-up IOP value decreased to 14.93±2.25 mmHg in the first month (p=0.00). When OCTA images taken before and the first month after treatment were compared, it was determined that the early treatment diabetic retinopathy study (ETDRS) value for the outer nasal section significantly increased (p=0.042). There was no significant difference in the remaining parameters showing macular vessel density.

Discussion: LBN 0.024% is a topical ocular hypotensive agent effective in lowering IOP in the early period in patients with POAG.

Keywords

Glaucoma, Latanoprostene Bunod, Nitric Oxide, Optical Coherence Tomography Angiography

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Corresponding Author: Kemal Bayrakçeken, Department of Ophthalmology, Faculty of Medicine, Erzincan Binali Yildirim University, Erzincan, Turkey.
E-mail: kbayrakceken2006@hotmail.com P: +90 505 944 19 44
Corresponding Author ORCID ID: https://orcid.org/0000-0001-9550-1358
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Introduction

Glaucoma is a chronic, progressive optic neuropathy that can lead to vision loss and blindness [1]. Being the second leading cause of blindness worldwide, glaucoma is predicted to affect 111.8 million people by 2040 [2]. The main goal in the treatment of glaucoma is to slow down optic nerve damage and visual field deterioration by reducing intraocular pressure (IOP) [3]. Anti-glaucoma eye drops lower IOP by reducing aqueous humor production or increasing aqueous humor outflow from the trabecular meshwork or uveoscleral pathways. There are also eye drops that use both methods at the same time [4].

Prostaglandin analogs (PGAs) are widely used drugs in the initial treatment of primary open-angle glaucoma (POAG) [5]. PGAs are first-line drugs in the medical treatment of glaucoma due to their efficacy in lowering IOP, once-daily administration, and improved safety profile compared to other anti-glaucomatous therapies [6]. Studies have shown that these agents reduce IOP by increasing drainage of the aqueous humor via the uveoscleral route [7]. However, in some patients with glaucoma, PGAs fail to adequately control IOP and thus prevent disease progression [8]. These cases require the use of multiple agents with different mechanisms of action or complementary therapies [9].

Topical latanoprostene bunod (LBN) 0.024% (Vyzulta®; Bausch+Lomb; Bridgewater, NJ, USA), which has recently been increasingly used in clinical settings, is a nitric oxide (NO)-donating prostaglandin F2α analog. LBN is metabolized to latanoprost acid and butanediol mononitrate, and the latter is also metabolized to 1,4 butane diol and NO [10]. Unlike other IOP-lowering PGAs, LBN contains two active metabolites with different mechanisms of action. It increases the aqueous humor outflow of the uveoscleral pathway through the effect of latanoprost acid and the Trabecular meshwork/Schlemm canal through that of NO [11]. The VOYAGER study showed that LBN 0.024% resulted in a higher drop in the IOP than latanoprost 0.005%, which was attributed to the NO content of LBN [12]. Furthermore, the APOLLO and LUNAR studies reported that LBN 0.024% led to a greater reduction in the IOP compared to timolol 0.5% [13,14].

Although several studies have evaluated the effect of LBN 0.024% ophthalmic solution on IOP, there are still limited data concerning the effect of this agent on macular vascularity [12-14]. Therefore, in this study, we aimed to determine the effect of LBN on IOP and changes in macular vessel density in the early period using optical coherence tomography angiography (OCTA) in treatment-naive patients with POAG.

Material and Methods

This retrospective study included 46 eyes of 46 patients aged 40-60 years with newly diagnosed early/mild stage POAG on examination and imaging (retinal nerve fiber layer changes +, no abnormalities visual field). At the first visit, all study participants underwent detailed ophthalmological examination, including medical history, best-corrected visual acuity, slit-lamp biomicroscopy, iridocorneal angle assessment using gonioscopy, fundoscopy, and IOP measurement using Goldmann applanation tonometer (GAT), and findings were recorded. The eyes were anesthetized using 0.5% Alcaine solution (Alcon Laboratories Inc., Fort Worth, TX, USA), and a fluorescein strip was applied to the inferior conjunctival fornix and then GAT (AT900; Haag Streit Diagnostics, Köniz, Switzerland) measurements were taken using cobalt blue filter of biomicroscope. All IOP measurements were made in the morning hours. Central corneal thickness (CCT) of patients was measured using the Nidek AL-Scan instrument (Nidek CO., Gamagori, Japan). Retinal imaging was performed using Nidek's RS300 Advance OCTA device (Nidek Co. Ltd., Gamagori, Japan), a non-invasive retinal imaging device. All measurements were made by the same person (KB).

Participants were selected from patients who used LBN as monotherapy (Vyzulta, Bausch+Lomb, USA) once a day. IOP values and OCTA findings in the early (first-month) follow-up of the same patients were screened from the archive and compared with the data that had been obtained at the time of their first presentation. Patients with a history of corneal ocular surface disease, those with a history of using ocular or systemic corticosteroids that could affect IOP, those with a history of topical ocular hypotensive drug use, and those who had undergone any eye surgery were excluded from the study. None of the study participants had systemic disease.

Macular thickness (in nine quadrants defined by the Early Treatment Diabetic Retinopathy Study (ETDRS)) [15] and ganglion cell complex thickness were measured using OCT (Nidek Co. Ltd., Aichi, Japan). In addition, foveal avascular zone parameters (area, circumference, and circularity index) in the macular region and the vessel density (VD) values of the outer and inner portions of the superficial capillary plexus (SCP) were measured using OCTA.

Ethical approval was obtained from the Clinical Research Ethics Committee of the Erzincan Binali Yıldırım University (27-04-2023, decision No: 2023/09-1). Written informed consent was obtained from all participants who participated in this study.

Statistical Analysis

Data analysis was performed using the Statistical Package for the Social Sciences (IBM SPSS) v. 25. The conformity of continuous variables to the normal distribution was examined with the Shapiro-Wilk test and kurtosis-skewness values. Continuous variables were expressed as mean ± standard deviation and categorical variables were expressed as percentages and frequencies. To determine whether the difference between the measurements was significant, a paired-sample t-test analysis was performed. The significance value was set at $p < 0.05$.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

The mean age of the patients participating in the study was 52.06 ± 7.38 (range 40-60) years. Twenty-three (50%) participants were male, and 23 (50%) were female.

At the time of the first presentation, the mean CCT value was 549.1±16.3 μ, the mean IOP value of the patients was 26.20±2.84 mmHg, which statistically significantly decreased to 14.93±2.25 mmHg in the first month after LBN monotherapy (t44: 9.16; p=0.00).

When the OCTA images of the patients taken before and after treatment were evaluated, it was determined that the ETDRS value for the outer nasal section significantly increased in the first month after treatment (t45: 2.22; p=0.042). However, there

was no significant difference between the pre-treatment and post-treatment first-month values obtained for the remaining parameters (Table 1) (Figures 1-3).

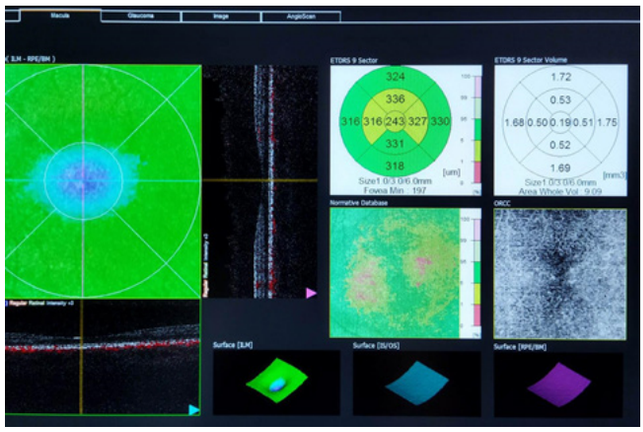

Figure 1. Measurement of the macular thickness according to the ETDRS chart using Nidek's RS-3000 Advance and Navis Ex. Ver. 1.1.5 software.

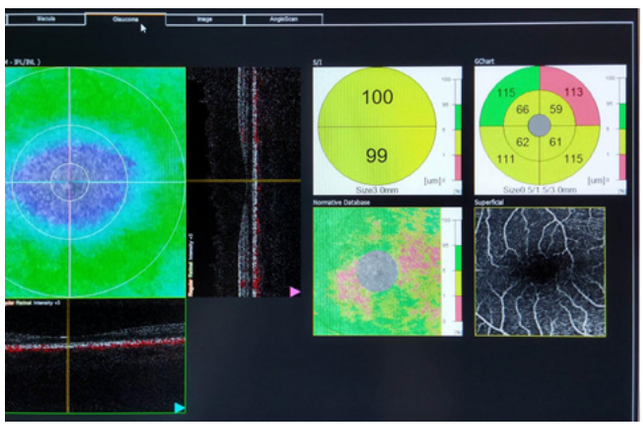

Figure 2. Superior and inferior ganglion cell complex thicknesses.

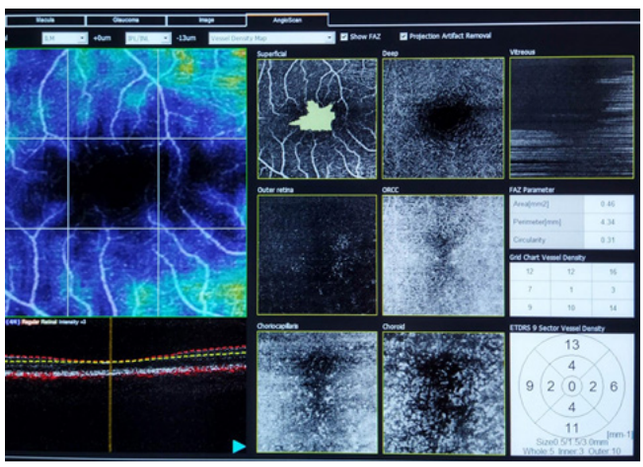

Figure 3. Foveal avascular zone metrics and vessel density values automatically measured by AngioScan software. The software only calculates the VD metrics at the level of the superficial capillary plexus.

Table 1. Comparison of patients' pre-treatment and post-treatment first-month OCTA values.

	Measurement	Difference between before treatment and first month after treatment Mean ± SD	P value
ETDRS, outer	Superior	-4.467 ± 29.053	.520
	Nasal	-5.100 ± 8.593	.042*
	Inferior	-5.500 ± 10.211	.084
	Temporal	.287 ± 13.256	.954
ETDRS, inner	Superior	-6.500 ± 14.999	.120
	Nasal	-2.767 ± 7.537	.182
	Inferior	-6.123 ± 18.847	.240
	Temporal	-3.167 ± 5.899	.074
CMT	CMT	4.077 ± 18.317	.414
GCC	Superior	-1.477 ± 5.986	.369
	Inferior	-2.367 ± 8.368	.316
FAZ	Area	.286 ± 2.756	.793
	Perimeter	.396 ± 3.041	.731
	CI	.036 ± .175	.670
ETDRS 9 sectors VD outer	Superior	-.743 ± 8.376	.837
	Nasal	-.943 ± 8.934	.792
	Inferior	-3.167 ± 9.655	.339
	Temporal	-1.543 ± 9.225	.626
ETDRS 9 sectors VD inner	Superior	.077 ± 7.066	.981
	Nasal	1.153 ± 6.536	.534
	Inferior	-1.943 ± 8.498	.493
	Temporal	-2.143 ± 6.535	.230
ETDRS	Central	-.4.667 ± 3.795	.651

SD: standard deviation, ETDRS: Early Treatment Diabetic Retinopathy Study (macular thickness map) score, CMT: central macular thickness, GCC: ganglion cell complex, FAZ: foveal avascular zone, peri; perimeter, CI: circular index, VD: vessel density; *p < 0.05

Discussion

In this study, we investigated the effect of using LBN-containing drops as monotherapy on IOP and macular vessel density in treatment-naive patients with POAG. We found that although LBN significantly reduced the IOP in the acute phase (first month), it did not affect macular vessel density.

While an increased IOP is the most important risk factor associated with glaucoma, there are studies showing that blood pressure, vasospasm, and ocular blood flow also play a role in the pathogenesis of this condition [16]. OCTA is a non-invasive imaging modality used to evaluate retinal and optic nerve head vascularity in glaucomatous eyes [17]. OCTA studies have revealed decreased superficial vessel density in the peripapillary and macular areas, as well as choriocapillaris losses in areas of parapapillary atrophy, in patients with POAG [18]. Various studies have investigated the effect of topical ocular hypotensive drugs on the optic nerve head and retinal and choroidal microcirculation [19,20]. Liu et al. reported that topical latanoprost treatment had no ameliorative effect on macular blood flow in previously untreated glaucoma patients [21]. Similarly, Chen et al. found no change in foveal vessel density in patients treated with latanoprost 0.005% ophthalmic solution for four weeks, although they detected an increase in peripapillary vessel density [22]. It can be considered that medical treatment of glaucoma does not affect macular vessel density. Despite the lack of sensitivity of macular vessel density, significant changes in blood flow in the peripapillary area may

provide more valuable information on the pathogenesis of glaucoma.

Although El-Nimri et al. found that LBN significantly increased macular vessel density, they found no statistically significant difference in peripapillary vessel density [23]. In contrast, we detected no significant change in macular vessel density after LBN therapy. NO has been reported to play a neuroprotective role by causing changes in the optic nerve, retina, and choroidal blood flow [24]. The reason for the increase in macular vessel density may be the vasodilator effect of the NO molecule; however, it is not possible to determine the exact cause. Future studies on the bioavailability of the NO molecule in LBN in the posterior segment may provide valuable data to elucidate this issue.

Study limitations

Our study had some limitations. First, our study had a short follow-up period. Longer follow-ups of patients may better reveal the relationship between macular microvasculature and the IOP decrease. Second, vascular density of the peripapillary region was not evaluated. Finally, the number of participants should be increased for a better interpretation of the findings.

Conclusion

LBN 0.024% is a safe and effective anti-glaucomatous eye drop that significantly reduces the IOP in the early period when used as monotherapy in patients with POAG. It also does not seem to have any effect on foveal vessel density. In addition, the eyes were similar in terms of clinical parameters (CCT, etc.) However, there is a need for longer follow-up studies to clarify the relationship between LBN therapy and macular vessel density.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of interest

The authors declare no conflict of interest.

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